

In re Application of: Anthony FUTERMAN et al.
Serial No.: 10/552,287
Filed: January 4, 2007
Final Office Action Mailing Date: April 8, 2009

Examiner: David J. STEADMAN
Group Art Unit: 1656
Attorney Docket: 30227

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 123, 124, 129, and 133-156 are pending in the Application. Claims 139-156 have been withdrawn from consideration. Claims 123, 124, 129 and 133-138 have been rejected.

Claims 123, 124, 129 and 133-138 have been rejected under 35 U.S.C. §112. Claims 133-137 have been rejected under 35 U.S.C. §102(a) as anticipated by Dvir et al. Claim 138 has been rejected under 35 U.S.C. §103(a) as being obvious over Dvir et al. Claims 123, 129, 133-136 and 138 have now been amended. New claims 157 and 158 have been added herewith.

Declaration

The Examiner has alleged that the Applicants' Declaration under 37 C.F.R. §1.132 cannot be located in the Applicants' file. Applicants regret the apparent misplacement of the Declaration, which was submitted on December 17, 2008, along with the Response to the Office Action mailed September 17, 2008. Please see the attached cover page with mail room stamp dated December 17, 2008 for confirmation of receipt. Nonetheless, Applicants provide herewith a copy of the executed Declaration of Anthony FUTERMAN, which asserts that Andrew A. MCCARTHY was not a co-inventor of the above-identified Application, for entrance into the record and consideration by the Examiner. A later version of this Declaration, revised to include signatures of all the instant inventors, is presently being executed and will be provided for entrance into the record in the near future. A copy of this *unexecuted* Declaration is attached herewith for your convenience.

Claim to Priority

While traversing the Examiner's assertions, Applicants have chosen to amend the Domestic Priority paragraph with regard to US Provisional Patent Application No. 60/463,049, in accordance with the Examiner's requirements.

Regarding Foreign Priority, the Examiner has acknowledged that PCT Application No. PCT/IL2004/000335 clearly provides support for the subject-matter

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of claims 123-124, 129 and 133-138, and that Israel Patent Application No. 156273 clearly provides support for the subject-matter of claims 123-124 and 129.

New claims 157 and 158 relate to the glucocerebrosidase solutions of claim 129, having normal enzymatic activity (157) and in a pharmaceutical composition for treating Gaucher's disease (158). Applicant submits that claims 157 and 158 are fully supported in the disclosure of Israel Patent Application No. 156273, as indicated by the Examiner (*see* Final Office Action dated April 8, 2009, pages 4 and 5), and thus derive benefit of priority therefrom (June 2, 2003).

Specification/Informalities

Applicants have amended the Specification to include the substitute Sequence Listing paper copy filed on January 4, 2007, as required by the Examiner (*see* "In the Specification", *supra*).

35 U.S.C. §112, First Paragraph Rejections

The Examiner has rejected claims 123-124, 129 and 133-138 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner's rejections are respectfully traversed. Claims 123, 129, 133-136 and 138 have now been amended.

Regarding claims 129 and 133-138, claim 129, and claims dependent therefrom have now been amended to recite "...glucocerebrosidase solution..." in place of "glucocerebrosidase preparation...", thereby limiting the claim to non-crystalline glucocerebrosidase. Support for such an amendment is found throughout the instant specification, for example, Example 1:

"Crystals were obtained via the hanging-drop technique at room temperature using a drop composed of 1.5 microliters of the 10 mg/ml glucocerebrosidase solution and 1.5 microliters of mother liquor [1 molar (NH₂)₂SO₄ pH 4.6, 0.17 molar guanidine hydrochloride, 0.02 molar KCl, 0.1 molar sodium acetate buffer, pH 4.6]." (page 80, lines 17-20 of the instant specification)

Regarding claims 123-124, 129 and 133-138, claims 123 and 129 have now been amended to recite the phrase "...consisting of the amino acid sequence as set

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forth in SEQ ID NO: 1...", in place of the phrase "...having the the amino acid sequence...", thereby further defining the claimed "glucocerebrosidase molecule".

Regarding the predictability of crystallization, Applicants maintain that claims 123 and 129 read on clearly defined glucocerebrosidase polypeptide molecules, which can form crystal structures having characteristic structural coordinates, space group and unit cell dimensions. That notwithstanding, and in order to expedite prosecution in this case, Applicants have chosen to amend claims 123 and 129 to include the protocol for preparation of glucocoerbrosidase solution for crystallization, as detailed in Example 1 of the instant specification (*see* page 80, lines 5-16 of the instant specification):

"...and wherein said glucocerebrosidase molecule is prepared by: dialysis overnight against phosphate-buffered saline (PBS) pH 7.0; deglycosylation of said glucocerebrosidase with N-glycosidase F; concentration of said glucocerebrosidase to 10 mg/ml in 1 millimolar 2-morpholinoethanesulfonic acid (MES) pH 6.6, 0.1 molar NaCl, 0.02 % NaN₃ by centrifugal concentration using a 10 kDa cut off filter..."

thereby further defining the characteristics of the claimed crystalline structure and polypeptide, and relevant parameters for making such.

Thus, Applicants submit that now amended claims 123 and 129 read on clearly defined glucocerebrosidase polypeptide molecules, which can form crystal structures having characteristic structural coordinates, space group and unit cell dimensions, which glucocerebrosidase polypeptides and crystals are supported, and thus fully enabled throughout the instant specification.

102(a)/103(a) Rejections: Dvir et al. (EMBO Reports, 2003; 4:704-709)

The Examiner has rejected claims 133-138 under 35 U.S.C. §102(a) and §103(a) as anticipated by [102(a)] or obvious [103(a)] over Dvir et al. The Examiner's rejection is respectfully traversed. Claims 123, 129, 133-136 and 138 have now been amended.

Applicants are attaching an executed Declaration under 37 C.F.R. §1.132, in which Prof. Anthony H. Futerman asserts that the co-author, Andrew A McCarthy, identified along with Hay Dvir, Michal Harel, Lilly Toker, Israel Silman,

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Anthony H. Futerman and Joel L. Sussman in an article entitled *X-Ray Structure of Human Acid-Glucosidase, the Defective Enzyme in Gaucher Disease*, published on June 3, 2003 (online publication) in "EMBO Reports" in Vol. 4, Issue 7, at pages 704-709, was identified as a co-author on said article along with Hay Dvir, Michal Harel, Lilly Toker, Israel Silman, Anthony H. Futerman and Joel L. Sussman for his collaborative efforts operating under our guidance and direction, and was not a co-inventor of the above-identified application. The Declaration further asserts that the only inventors of the invention are Hay Dvir, Michal Harel, Lilly Toker, Israel Silman, Anthony H. Futerman, Svetlana Adamsky and Joel L. Sussman.

As such, the above-identified publication cited by the Examiner to reject claims 133-138 is not a publication of "another", but rather Applicants' own publication, which was published less than a year before Applicants' filing date, and thus is not proper prior art thereagainst.

Thus, Applicants respectfully request withdrawal of the rejection on the basis of §102(a)/§103(a).

In view of the foregoing amendments and remarks, pending claims 123, 124, 129, 133-138 and new claims 157 and 158 are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Respectfully submitted,



Martin D. Moynihan
Registration No. 40,338

Date: July 8, 2009

Enclosures:

- Additional Claims Fee Transmittal;
- Copy of Executed Declaration of Anthony FUTERMAN;
- Copy of Mail Room Stamp dated December 17, 2008;
- Unexecuted Declaration listing all of the instant Inventors; and
- Substitute Sequence Listing paper copy and Floppy Disc